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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/731,632	11/20/2000	Wanda A. Cromlish	43639.010400	3503

7590 10/25/2004

Eugene C Rzucidlo Esq
Greenberg Trauriq LLP
885 Third Avenue 21st Floor
New York, NY 10022

EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 10/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/731,632	CROMLISH ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,19 and 22-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,19 and 22-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9-1-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *appendix*.

DETAILED ACTION

Reissue Application

Claims 1-15, 19, 22-27 are currently pending in this re-issue application.

Applicants' amendments and arguments filed on 9-1-04, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. However, new rejections/objections are now in place.

Applicant is reminded of the continuing obligation under 37 CFR 1.178(b), to timely apprise the Office of any prior or concurrent proceeding in which Patent No. 5,543,297 is or was involved. These proceedings would include interferences, reissues, reexaminations, and litigation.

Applicant is further reminded of the continuing obligation under 37 CFR 1.56, to timely apprise the Office of any information which is material to patentability of the claims under consideration in this reissue application.

These obligations rest with each individual associated with the filing and prosecution of this application for reissue. See also MPEP §§ 1404, 1442.01 and 1442.04.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that applicants do not provide specific SEQ ID NO to the sequences depicted

in the drawings either on the drawings or in the figure description. Furthermore in response to the previous reminder to comply with sequence rules by filing or requesting the transfer of the electronic form of the sequence information from the parent application to the instant re-issue application to the STIC library, applicant makes a request under the remarks section for transfer of the sequences from the parent to the instant application. However, such a request is improper and the applicant is urged to make the request on a separate sheet of paper and use the form paragraph enclosed here with as an appendix. Examiner also urges applicant to see particularly 37 CFR 1.821(d) and (e).

Applicant is notified that any subsequent amendment to the specification and/or claims must comply with 37 CFR 1.173(b).

Information Disclosure Statement

Examiner acknowledges the filing of the information disclosure statement and Form 1449. A copy of the signed Form 1449 is enclosed herewith.

Submission of the Original Patent

Applicants have not submitted the original patent. The original patent, or a statement as to loss or inaccessibility of the original patent, must be received before this reissue application can be allowed. See 37 CFR 1.178.

In response to the previous Office action, applicant has requested that this issue be held in abeyance until allowable subject matter is defined.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 19, 26-27 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 19, 26-27 are drawn to "a transformed host that expresses" which could read on a transformed human, a non-statutory subject matter. While applicant may argue that the word "transformed" shows the hand of man, such an argument is still not persuasive to overcome the rejection because transforming a human by itself is a non-statutory subject matter. Amending the claim to recite "a transformed host cell that expresses" which appears to be the actual intention of the applicant, would overcome the above rejection.

Applicant is notified that any subsequent amendment to the specification and/or claims must comply with 37 CFR 1.173(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6-7, 11, 14, and claims 4-5, 12-13, 15 which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-3, 6-7, 11 and 14 are drawn to an assay for determining the COX-2 activity "of a sample" comprising the steps of adding a cell preparation, a sample comprising a COX-2 inhibitor and arachidonic

acid followed by measuring the amount of PGE produced. The step (a) is highly confusing to the Examiner because it is not clear whether the "sample" in the preamble of the claims and the "sample" in step (2) of (a) are one and the same. If they are one and the same, then it is not clear to the Examiner as to how one of ordinary skill in the art can expect to test the activity of the sample having an inhibitor of the enzyme. It is not clear whether applicants meant to claim and assay to determine the COX-2 *inhibitory* activity of a sample, wherein said sample comprises a putative COX-2 inhibitor. On the other hand if applicant did not mean the above, Examiner requests clarification.

Applicant is notified that any subsequent amendment to the specification and/or claims must comply with 37 CFR 1.173(b).

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 14 recites the limitation "a sample according to claim 10" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Applicant is notified that any subsequent amendment to the specification and/or claims must comply with 37 CFR 1.173(b).

Claims 19, 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 19, 22-25 all refer to sequences in figures and recites specific SEQ ID NO in parentheses. Such a depiction is confusing and unclear to the Examiner. This is

because applicants do not provide a SEQ ID NO for the sequences depicted in the figure and therefore it cannot be taken for granted that the sequences in the figures and those listed in the sequence listing with appropriate SEQ ID NO are one and the same. Examiner urges applicants to refrain from referring sequences to the figure and provide only SEQ ID NO. Correction is required.

Applicant is notified that any subsequent amendment to the specification and/or claims must comply with 37 CFR 1.173(b).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19, 22-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 19, 22-25 are directed to humancycloxoygenase-2 cDNA with SEQ ID NO:11 and purified, recombinant or isolated human cyclooxygenase-2 polypeptide having an amino acid sequence SEQ ID NO:10. Claims 16-25 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from humans that have not been disclosed in the specification. The examiner maintains the position that the single representative disclosed species, i.e., the polypeptide with SEQ ID NO:10 and the polynucleotide with SEQ ID NO:11, fails to represent the entire genus of claimed human cyclooxygenase-2 polypeptides (underline added for emphasis).

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. In the instant specification, a single human COX-2 polypeptide is described as SEQ ID NO:10, (which is encoded by SEQ ID NO:11) having prostaglandin synthase activity. This description also adequately describes a genus, within the sequence identity limitation of the instant claims, of polypeptides having this particular function. Those sequences that are "human" are a subset of this genus of polypeptides/polynucleotides having greater than 95% amino acid sequence identity to SEQ ID NO:10/11 and having said activity. The specification fails to define those structural features of SEQ ID NO:10/11 that are commonly possessed by members of the genus that distinguish them from other "non-human" polypeptides. Thus, one skilled in the art cannot visualize or recognize the identity of the members of the genus. As such, this single representative species does not adequately describe this subset according to its structure so that one of skill in the art can visualize and distinguish those amino acid sequences that are human, particularly in view of the larger genus that includes both human and non-human sequences. Therefore, the instant claims are not adequately described.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants submit that they have canceled claims 16-18 and 20-21 and hence the rejection is rendered moot. Examiner respectfully disagrees with such an argument. While Examiner acknowledges that claims 16-18, 20-21 have been cancelled and the rejection is rendered moot only to those claims, other claims such as claims 19, 22-25 are still directed to "human" polypeptides and applicants have not addressed these claims. Hence the rejection is maintained.

Applicant is notified that any subsequent amendment to the specification and/or claims must comply with 37 CFR 1.173(b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rodan et al. (J. Bone Mineral Res. 1986, Vol. 1(2):213-220 cited in Form 1449). Claim 8 in this instant application is drawn to a composition comprising an osteosarcoma cell preparation having 10^3 to 10^9 cells per c.c. of preparation or 50-500 micro gram of osteosarcoma microsomes and 01. to 50 micro liters of arachidonic acid per c.c. of cell preparation.

Rodan et al. teach several types of human osteosarcoma cell and provide cell culture composition of the same. The reference also teaches the use of said cells for assay of COX activity along with exogenous use of arachidonic acid in such reactions. Rodan et al. actually investigate the basis for differences in prostaglandin synthesis among osteosarcoma cell lines and examine the effect of a number of bone resorbing agents on prostaglandin production and report that the differences in PGE synthesis between osteoblastic and non-osteoblastic rat osteosarcoma cells were associated with COX dependent release of arachidonic acid.

With the above teaching of Rodan et al. in hand, it would have been obvious to those skilled in the art to make several types of cell preparations to study the above aspects, one of which would be a cell preparation between 10^3 or 10^5 or 10^9 (as required) osteosarcoma cells per c.c. along with varying amounts of arachidonic acid such as 0.1 to 50 or 100 micro liters. One of ordinary skill in the art would have been motivated to do so in order to set up reactions to study the effects of bone resorbing agents on PGE synthesis. One of ordinary skill in the art would have a reasonable expectation of success since Rodan et al. provide the cells and a detailed information regarding their role and their physiology.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

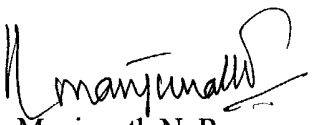
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao
October 1, 2004